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REMARKS

Claim 1 has been amended by incorporating the following definitions:

for R_2 , R_1 and R_{1j} : the definition at page 28, line 10 to page 31, line 20;

for X-X: the definition at page 11, lines 3 to 4 and also in Claim 15 (now canceled);

for L: the definition in Claim 6 (now canceled);

for R_3 : the definition at page 13, line 22 to page 14, line 32;

for Cy and R_{3a} : the definition of Cy in Claim 17 (now canceled); the definition of R_{3a} at page 20, line 22 to page 22 line 4; and three specific values for Cy in the list of examples of specific values at page 24, line 30 to page 25, line 10. The three specific values for Cy are illustrated in Examples 81, 89 and 98.

Since the definition of Cy now includes 2-trifluoromethylthiophenyl, the reference to the specific 2-trifluoromethylthiophenyl compound named at the end of the claim, which is exemplified in the application, has been deleted.

Claim 2 has been amended by incorporating the definition of Cy from original Claim 18 (deleting those values falling outside the scope of the Examiner's restriction requirement). The claim has also been simplified by deleting definitions common to Claim 1.

Claim 2 is believed to be wholly entitled to the priority date of PCT/GB00/02302. Support for the values listed for Cy may be found at page 31, lines 1 to 7. Support for the values listed for R_{3a} may be found at page 31, line 8 to page 32, line 13.

Several claims have been canceled and the dependency of Claim 25 adjusted accordingly.

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Claim 29 has been amended to recite the specific thrombotic disorders listed at page 2, lines 21 to 34 of the description. It has also been amended to recite definitions of groups as in Claim 1. Since the definition of Cy now includes 2-trifluoromethylthiophenyl, the reference to the specific 2-trifluoromethylthiophenyl compound named at the end of the claim, which is exemplified in the application, has been deleted.

Claims 32 and 34 have been amended as a consequence of the amendments in Claim 1.

New Claim 37 is supported by the list of examples for specific values for Cy at page 24, line 30 to page 25, line 10 (deleting those falling outside the scope of the Examiner's restriction requirement).

PRIORITY

The Examiner has asserted that Applicants' claim to priority from PCT/GB/02302 cannot be recognised. The Examiner does not provide reasons in the Office Action.

Applicants respectfully submit that the present application is entitled to claim priority from PCT/GB00/02302. Compounds claimed in the present application were first disclosed in that PCT application.

Referring to the first 53 Examples, many of these were first disclosed in the '2302 PCT application, as tabulated below.

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Example	'2302	Example	'2302	Example	'2302
1a	201	26	-	50	261
1b	-	-	-	51	262
2	202	27	-	52	265
3	203	28	-	53	266
4	204	29	-		
5	205	30	-		
6	206	31	-		
7	207	32	-		
8	208	33	-		
9	209	34	-		
10	210	35	-		
11	-	36	-		
12	211	37	-		
13	212	38	-		
14	213	39	-		
15	-	39a	-		
16	-	40	214		
17	-	41	215		
18	-	42	216		
19	-	43	217		
20	-	44	218		
21	252	45	219		
22	253	46	220		
23	-	47	258		
24	-	48	259		
25	-	49	260		

The compounds claimed in the present application were also disclosed generically in the PCT/GB00/02302. Thus, for example, the general formula for $Lp(D)_n$ in the claims was described at page 12, line 3 to page 13, line 7 and in Claim 14. The Examiner will note that in the presently claimed

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compounds, X_a in the general formula for $L_p(D)_n$ is CH and X_b is N. These features distinguish the claimed compounds from those described in the priority documents for PCT/GB00/02302.

DOUBLE PATENTING

Claims 1-15, 17, 18, 21-26, 29 and 32-36 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims of co-pending application no. 09/926,712 filed December 6, 2001.

Applicants respectfully submit that the present claims are patentably distinct from the compounds claimed in of co-pending application no. 09/926,712.

The co-pending application is the national stage of PCT/GB00/02302, from which the present application claims priority. The claims in that national stage application have been amended so that they do not overlap with the claims in the present application. The Examiner is asked to note in particular that the presently claimed compounds all possess an $L_p(D)_n$ group in which X_a is CH and X_b is N. None of the compounds claimed in the co-pending application contain such an $L_p(D)_n$ group.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-15, 17, 18, 21-26, 29 and 32-36 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being unclear. Applicants respectfully submit that the claims as amended comply with 35 U.S.C. § 112, second paragraph.

In the amended claims, the bridge -X-X- has been defined as -CONH-. However, it is respectfully submitted that the original definition for -X-X- satisfied the requirements of 35 U.S.C. § 112, second paragraph. Thus, the definition

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contemplated the possibility of single, double and triple bonds between each atom or group represented by X.

It is respectfully submitted that the definition of Cy as amended satisfies the requirements of 35 U.S.C. § 112, second paragraph.

The term "optionally substituted" has in general been deleted, but has been retained in the definition for Cy in Claim 1. Applicants respectfully submit that the invention is not limited to compounds having specifically defined alternative numbers and points of attachment of R_{3a} to Cy. Indeed, but for the Examiner's restriction requirement, Applicants would have sought to retain a definition for Cy that includes heterocyclic groups. The Examples illustrate a wide diversity of possible values for Cy.

The definition of L has been amended.

The term "and/or" has been retained in parts of the claims where it is believed to be clear and to provide the most concise language. Thus, it is believed that the claims as amended are clearly directed to a single compound, not to mixtures of compounds.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

Claim 29 stands rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement.

It is respectfully submitted that Claim 29 as amended satisfies the requirements of 35 U.S.C. § 112, first paragraph.

The compounds according to the present invention are Factor Xa inhibitors useful in the treatment of thrombotic disorders, as described at page 2, lines 21 to 34 of the description. Applicants state, at page 167, lines 4 to 6 that "In general, the compounds of formula (I) exemplified herein have been found to exhibit a K_i of 10 μM or less in Assay 1

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and/or a K_{ass} of at least 0.1×10^6 L/mole in Assay 2." It is understood that the Examiner recognises that this activity supports the presently claimed methods of use.

ALLOWABLE SUBJECT MATTER

The Examiner has indicated that the compound and pharmaceutical composition claims would be allowable if rewritten to overcome the rejections under 35 U.S.C., second paragraph, and comments that US 5,346,907 is considered to be the closest prior art.

For completeness of the record, Applicants would like to note they do not necessarily agree with the Examiner that US 5,346,907 represents the closest prior art, but that the issue is moot. Thus, the Examiner has properly evaluated the claimed invention with respect to each prior art reference as an entirety and with respect to all of the prior art as a whole and found the subject matter allowable. Accordingly, there is no requirement to establish any particular individual reference as the closest prior art.

It is noted that the compounds of the present invention are distinguishable structurally from those of US 5,346,907 by fact that X_a and X_b in the group $-L_p(D)_n$ of the instant application represent, respectively, CH and N. Thus, when r is 2, the moiety formed is a 1-substituted piperidin-4-yl group. However, the compounds of US 5,346,907 can contain a piperidin-1-yl group (see Example 61), but not a piperidin-4-yl group. Also, the compounds of US 5,346,907 are disclosed as CCK antagonists.

Further, WO 99/11658 and WO 99/11657, acknowledged in the introduction to the present specification, disclose compounds which are Factor Xa inhibitors; and WO 99/25686 (drawn to a totally different utility) includes a species which has been excluded from Claim 1; so any of them might be

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considered to be closer prior art. As noted above, there seems to be no need to resolve this point.

CONCLUSION

Applicants respectfully submit that the claims as amended define patentable subject matter. A Notice of Allowance is earnestly sought.

FUTURE COMMUNICATION BY TELEPHONE

If the Examiner wishes to speak by telephone with the undersigned in the future, the undersigned can be contacted by e-mail at martinahay@martin-a-hay.com, and would be pleased to telephone the Examiner in response. Alternatively, the Examiner can contact Linda McDonald at (317) 433 7140 and leave a message, which will be forwarded to the undersigned.

Respectfully submitted,



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 16, 2004